

REMARKS

Status of the Claims

Claims 6, 7, 9-43, 49-59, 61, and 62 are pending. Claims 22-43, and 49-54 are withdrawn. Claims 6 and 13 are amended above.

Examiner Interview Summary

A telephonic interview was conducted on December 18, 2008, between Examiner Pak and Applicants' representative. The interview is summarized on the Examiner Interview Summary form that the Examiner placed in the Record.

The time and attention of the Examiner during the interview are greatly appreciated.

There is now only one issue precluding allowance of this application, discussed below.

Issues Under 35 U.S.C. § 103

Claims 6-7, 9-21, and 55-62 are rejected under 35 U.S.C. § 103 as allegedly being obvious over Yu et al. in view of Taketo.¹ This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Both of these references and their many deficiencies with respect to the current claims are well-discussed in the record.

¹ The Office Action again indicates that the secondary reference is Tsujii. However, it is clear from the rejection that "Taketo" is intended.

The Office Action's Interpretation of Yu et al. is misplaced

In general, the Office Action states that Yu et al. disclose “a method of detecting/measuring COX-2 from a mammalian cell, by detecting/measuring a PGH₂-EA metabolites [sic]...” See page 4 of the Office Action. The Office Action further indicates that “one having ordinary skill in the art would have concluded to apply the method of Yu et al. in detecting COX-2 activity from a sample obtained from a living mammal.” *Id.* at page 5.

In general, Applicants respectfully submit that this is a mischaracterization of the reference. Additionally, the extrapolation the Office Action must take to allegedly establish obviousness is a flawed leap from both a scientific and obviousness standard standpoint.

First of all, in determining obviousness, §103 expressly requires considering the claimed invention “as a whole.” In looking at the claimed invention as a whole, one of ordinary skill in the art would first immediately notice there is a very distinctly different starting point.

As stated in the previous response, Yu et al. grow cultured cells, then actually induce COX-2 on order to determine if the cultured cells metabolize COX-2. This is a clear distinction between taking a sample from a living subject and using that sample to determine COX-2 activity in the subject. In other words, there is no reason for Yu et al. to determine the presence of COX-2, because they put it there in the first place.

Additionally, beginning with the induction of COX-2 in cultured cells does not permit one of ordinary skill in the art to “relate the amount of PGH₂-EA metabolites... to [a] disease state” as alleged on page 7 of the Office Action. Thus, the reference is not related to the present invention from a finishing point standpoint, either.

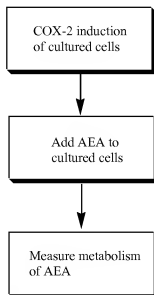
With a different “problem” at the beginning and a different “answer” at the end, relying on Yu et al. as a primary reference places the office the awkward position of acknowledging

many deficiencies. In fact, taking claim 6 as an example, in the four steps of the claim, the Office Action acknowledges that Yu et al. fail to teach three of the steps. See page 5 of the Office Action, which specifically states that “Yu et al. does [sic] not teach.”

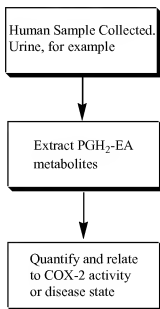
- “...a method of detecting an activity of COX-2 enzyme in a living mammal by obtaining a sample by a living mammal...”
- “the step of comparing the detected amount of PGH₂-EA metabolite to a previously determined amount from the mammal...”, and
- “the step over relating the amount of metabolites to a disease state or progression of a disease state...”

To further illustrate the differences in Yu et al. versus the present invention, consider the following diagrams which generally summarize the process of Yu et al. and an embodiment of the present invention.

The Process of Yu et al.:



Embodiment of the Present Invention:



The numerous differences between Yu et al. and the present invention create a very strained reliance on the secondary reference to remedy each and every one of said deficiencies.

The secondary reference, Taketo et al., is cited for establishing the notion “that COX-2 expression is increased in cancer cells, such as colon cancer cells...”. See the Office Action at page 5. Thus, the Office Action concludes that “with this knowledge in hand, one of ordinary skill in the art would have concluded to apply the method of Yu et al. to relate the amount of PGH₂-EA metabolites and thereby COX-2 activity to a disease state of progression of the disease state...” *Id.*

With this position, the Office Action is forced to make the unsupported allegation “that since Yu et al. teaches a method of selectively detecting COX-2 activity in a sample, one having

ordinary skill in the art would have concluded to apply the method of Yu et al. in detecting COX-2 activity from a sample obtained from a living mammal.” See page 5 of the Office Action. There is nothing in the prior art to support this misplaced assertion, and nothing in the prior art pointing to “reverse Yu et al.”

As indicated in the record, the prior art even teaches away from “reverse Yu et al.” At least as early as a prior response filed on December 26, 2006, Applicant has pointed out a specific section in Yu et al. that states that “at the present time the physiological significance of the metabolism of AEA by COX-2 is not known.” See Yu et al. at page 21186.

To date, the Examiner has chosen to ignore this aspect of Yu et al. The primary reference clearly explains, beyond the fact that Yu et al. did not even see a purpose for the metabolism of AEA by COX-2 that one of ordinary skill in the art would not look to Yu et al. as a means to arrive at the present invention, and that the measurements conducted in Yu et al. cannot be equated with the present claims. Additionally, it completely impeaches the Examiner’s position that one of ordinary skill in the art would look to Yu et al. to detect COX-2 activity from a sample obtained from a living mammal using the process of the present invention. As stated above, there is nothing in the Office Action to indicate otherwise.

Applicant’s respectfully submit that beyond looking to the prior art to determine if it suggests doing what the inventor has done, one must also consider if the art provides the required expectation as succeeding in that endeavor. See In re Dowell Chem. Co., 837 F.2d 469, 473 (Fed.Cir. 1988)(“both the suggestion and expectation as assessed must be founded in the prior art, not in Applicant’s disclosure”). In Yu et al.’s own words, it was clear there was no expectation to run this process in reverse to achieve the results desired by the Examiner.

Applicant's respectfully submit that one would not do so without the benefit of impermissible hindsight reconstruction based on the present application.

In reviewing the reference as a whole, it is no way to justify the statement that by detecting COX-2 activity in a sample of cells that are incubated with COX-2, one could have the other direction and detect COX-2 activity by detecting PGH₂ metabolites, particularly in view of the clear statement that the purpose of the presence of metabolites is currently not known.

The secondary reference fails to remedy the many deficiencies of Yu et al.

In the Office Action, Taketo is cited for the sole reason for showing "that COX-2 expression is increased in cancer cells, such as in colon cancer cells...". See page 5 of the Office Action.

Accordingly, Taketo fails to remedy the deficiencies stated in the Office Action that Yu et al. failed to "teach a method of detecting an activity of COX-2 enzyme in a living mammal by obtaining a sample from a living mammal..." Additionally, Taketo fails to disclose or suggest the step of comparing a detected amount of PGH₂ - EA metabolites to a previously determined amount from the mammal. Finally, Taketo fails to disclose or suggest any method "to detect COX-2 activity in a mammal by obtaining a sample from said mammal and detecting PGH₂-EA metabolites." (Page 7 of the Office Action.) Thus, Taketo fails to provide the strained nexus in the Office Action linking cells that have been induced with COX-2 in Yu et al. to obtaining a sample from a mammal and linking detected PGH₂-EA metabolites back to the presence of COX-2 activity. In other words, there is nothing in Taketo to remedy the statement in Yu et al.'s own words that the significance of the metabolism of AEA by COX-2 is not known.

The Examiner is mischaracterizing Applicant's prior argument

In the outstanding Office Action, in responding to previous arguments, the Examiner cites boilerplate language that “one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references...”. See page 7 of the Office Action. Applicants respectfully submit that it is very relevant to point out the many deficiencies of Yu et al. In fact, the Office Action itself even points to many. With so many deficiencies in the primary reference, Applicants are not “attacking references individually.” The secondary reference is cited to merely show that “COX-2 expression is increased in cancer cells,” so the “combination” is not a complicated one that relies heavily on the secondary reference. The secondary reference is not cited to show “how.”

Nothing in either reference would lead to claimed step (c).

Summary of the obviousness rejection

In summary, as stated above, there are five elements to the claimed method claims. The first step is obtaining a sample of the living mammal. Page 5 of the Office Action states that this is not taught by Yu et al. The next step is contacting the sample with a solvent to extract an amount of PGH₂-EA metabolite in the sample. Applicant's respectfully submit that since the process of Yu et al. first starts with COX-2 induction of cultured cells, there would be no reason to perform this step. The third step is quantifying an amount of extracted PGH₂-EA metabolites. Since there is no extracted PGH₂-EA metabolite associated with the Yu et al. process, this step is not disclosed as well. The fourth step is comparing the quantified amount to at least one of the standard, standard curve, or previously quantified amount. The Office Action acknowledges Yu et al.'s failure to teach this step. Finally, a fifth step is relating the quantified amount to a

diseased state or the progression of a disease state. The Office Action states that Yu et al. failed to disclose this step as well.

The Office Action attempts to overcome all the above deficiencies by the secondary reference's statement that "it is well established and known in the art that COX-2 expression is increased in cancer cells..."

Applicants respectfully submit that this argument does not rise to the level of obviousness.

Thus, Applicants submit that the above claims are free from the above rejection.

From the foregoing, further and favorable reconsideration in the form of a Notice of Allowance is requested and such action is believed to be in order.

If the Examiner has any questions concerning this amendment or the application in general, please contact the undersigned at the number listed below.

Respectfully submitted,



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